

Early changes in liver function could detect life-threatening infection

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Early changes in liver function detected by novel techniques can identify severe infection (sepsis) hours after onset and so could have important implications for the treatment of patients who are critically ill, according to a groundbreaking study by European researchers published in this week's *PLOS Medicine*.

Almost half of all people who develop severe sepsis die as this life-threatening condition often develops quickly and is often diagnosed too late to save the patient's life.

In this study, the authors from Austria, Germany, and the UK, led by Peter Recknagel from Jena University Hospital in Germany, used experimental laboratory work in [cell cultures](#), genetically modified mice and rats, and studies carried out in critically ill patients to shed light on the mechanisms behind severe sepsis.

They found that in animal models, [liver dysfunction](#) is an early sign of sepsis and that a process known as [PI3K](#) signalling (which is involved in several immune processes) plays a crucial role in the development of liver dysfunction. The authors also found that all aspects of detoxification by the liver are affected during sepsis, a finding which suggests that clinical outcomes are linked to the severity of these liver changes.

The clinical information included in the study from 48 patients with severe sepsis also supports the finding from the animal models and

suggests that [liver function tests](#) might help in the early diagnosis of sepsis and also provide information about possible clinical outcomes. As many medicines are broken down in the liver, these findings suggest that giving certain drugs to patients with severe sepsis may further damage the liver.

The authors explain their findings: "Liver dysfunction is an early and commonplace event in the rat model of sepsis studied here; PI3K signalling seems to play a crucial role. All aspects of hepatic biotransformation are affected, with severity relating to subsequent prognosis."

They continue: "Detected changes significantly precede conventional markers and are reflected by early alterations in plasma bile acids."

The authors conclude; "These observations carry important implications for the diagnosis of liver dysfunction and pharmacotherapy in the critically ill. Further clinical work is necessary to extend these concepts into clinical practice."

In an accompanying Perspective, John Marshall, a critical care expert from the University of Toronto (uninvolved in the study), says: "The hybrid translational model embodied in the work reported here by Bauer and colleagues not only provides a valuable new insight into the pathogenesis of liver derangements in sepsis, but even more importantly, establishes a model that should be welcomed and embraced by scientists working in the field."

More information: Recknagel P, Gonnert FA, Westermann M, Lambeck S, Lupp A, et al. (2012) Liver Dysfunction and Phosphatidylinositol-3-Kinase Signalling in Early Sepsis: Experimental Studies in Rodent Models of Peritonitis. PLoS Med 9(11): e1001338. [doi:10.1371/journal.pmed.1001338](https://doi.org/10.1371/journal.pmed.1001338)

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